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EDITORIAL

In this issue...

The potential of pluripotent human cells to differentiate into any adult cell type has captured the imagination of scientists and the public alike. One of the key human diseases targeted for cell replacement therapy is type I diabetes. In their review **Derivation of insulin-producing cells from human embryonic stem cells**, **Dennis Van Hoof**, **Kevin D'Amour** and **Michael German** review pancreatic development and discuss the current status of experiments in which human embryonic stem cells have been differentiated towards pancreatic endocrine lineages.

In their article **Governing stem cell banks and registries: Emerging Issues**, **Rosario Isasi** and **Bartha Knoppers** report the preliminary findings of a survey of stem cell banks participating in the International Stem Cell Forum's International Stem Cell Banking Initiative (ISCBI). The article provides an overview of the current international hESC banking landscape and provides a starting point for discussion surrounding key questions and challenges as concerns provenance, access, and deposit of hESC lines.

Transplantation of human embryonic stem cell-derived cardiomyocytes (hESC-CM) has been shown to transiently improve the function of the rodent heart one month after myocardial infarction. However, the mechanistic basis and optimal delivery strategies remains unclear. In their manuscript entitled **Improvement of mouse cardiac function by hESC-derived cardiomyocytes correlates with vascularity but not graft size, Linda van Laake** and colleagues from the laboratories of **Pieter Doevendans** and **Christine Mummery** investigated the influence of the number of injected cells, resulting graft size, and possible paracrine mechanisms. Transplantation of differentiated hESC-CM increased myocardial vascularization and enhanced heart function in mice after MI, but surprisingly, larger graft size was associated with reduced functional improvement.

Pluripotent human embryonic stem (hES) cells are capable of generating a variety of mature cell types, including hematopoietic cells in vitro. However, the precise signaling mechanisms that regulate hematopoietic cell development from hES cells are still poorly documented. In their paper **WNT and BMP signaling are both required for hematopoietic cell development from human ES cells, Yi Wang** and **Naoki Nakayama** demonstrate that hemoangiogenic cells derived from hES cells express high-level of KDR and low-level expression of PDGFRα, and that the generation of such cells from hES cells was significantly elevated by the addition of WNT3a or BMP4 during differentiation.

In a second paper from the same laboratory, entitled **BMP inhibition stimulates WNT-dependent generation of chondrogenic mesoderm from embryonic stem cells, Makoto Tanaka** and colleagues explore the generation of mesoderm from ES cells. Osteochondrogenic mesoderm expressed PDGFRα, and also genes that mark somites and rostral presomitic mesoderm. Exposure to high concentrations of WNT was required to generate these lineages, while lower concentrations of WNT3a were sufficient for specifying axial mesoderm.

In their article **Enhancement of human embryonic stem cell pluripotency through inhibition of the mitochondrial respiratory chain, Sandra Varum** and colleagues in the laboratories of **Joao Ramalho-Santos** and **Christopher Navara** report the results of experiments in which they inhibited the mitochondrial respiratory chain with antimycin in hESCs. PCR analysis demonstrated that the levels of Nanog mRNA were elevated 2-fold in antimycin A-treated cells, and antimycin A was able to replace bFGF in the media, as long as autocrine bFGF signaling was maintained. Antimycin A treatment reduced the expression of genes associated with differentiation, possibly acting through a ROS-mediated pathway.

Hidetoshi Sakurai and colleagues demonstrate methods for BMP4-mediated induction of paraxial mesodermal progenitors using PDGFR-α and E-CADHERIN as markers for purification and characterization in their paper entitled **Bidirectional induction toward paraxial mesodermal derivatives from mouse ES cells in chemically defined medium**. They report that serum-free monolayers of ESCs cultured with BMP4 induced paraxial mesodermal progenitors that could differentiate into osteochondrogenic cells whilst, early removal of BMP4 followed by lithium chloride (LiCl) promoted the differentiation to myogenic progenitor cells that were able to differentiate further in vitro into mature skeletal muscle cells.

Endoderm plays an inductive role in the formation of cardiomyocytes in many vertebrates. **Rian Nijmeijer** and colleagues from the laboratory of **Susana Chuva de Sousa**

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Lopes provide further evidence for this in their paper **Visceral endoderm induces specification of cardiomyocytes in mice**. They show that removal of the visceral endoderm reduced the formation of beating areas in embryo explants in culture and that coculture with the END2 cell line, which has visceral endoderm-like properties, restored the formation of beating areas. Similarly, they demonstrated enhanced cardiomyogenesis in mouse embryonic stem cells cultured in the presence of native visceral endoderm.